

REMARKS

Claims 4 and 22-28 are pending in the present application and under examination. In the Office Action mailed on November 13, 2008, all of the claims were rejected.

I. Rejection Under 35 USC 103

Claims 4, 22-26 and 28 are rejected under 35 U.S.C. § 103(a), as allegedly being unpatentable over the disclosure print out of the 'Contig295' sequence data from the sequence file 1997-12-15-NM.dbs attached to the Parkhill Declaration in view of the printed output from the NCBI open reading frame finder, Sambrook *et al.*, and Campbell AM.

Applicants respectfully traverse the rejection and its supporting remarks.

A. 1997-12-15-NM.dbs Has Not Been Established as Prior Art

The rejection is based on the supposed disclosure on a FTP server in late 1997 of a sequence named 'contig295' within a file named '1997-12-15-NM.dbs'. The evidence of this supposed disclosure is a declaration from Julian Parkhill, Ph.D., and its accompanying sequence printouts (2133 pages in total). Dr Parkhill does not mention where in particular 'contig295' might be found within these 2133 pages, but even if specific disclosure were provided the declaration does not provide sufficient facts to establish that 1997-12-15-NM.dbs is prior art under 35 U.S.C. § 102. Section 21028 of the MPEP discusses the requirement for being a "publication":

A reference is proven to be a "printed publication" "upon a satisfactory showing that such document has been disseminated or otherwise made available to the extent that persons interested and ordinarily skilled in the subject matter or art, exercising reasonable diligence, can locate it." *In re Wyer*, 655 F.2d 221, 210 USPQ 790 (CCPA 1981) (quoting *I.C.E. Corp. v. Armco Steel Corp.*, 250 F. Supp. 738, 743, 148 USPQ 537, 540 (SDNY 1966)) ("We agree that 'printed publication' should be approached as a unitary concept. The traditional dichotomy between 'printed' and 'publication' is no longer valid. Given the state of technology in document duplication, data storage, and data retrieval systems, the 'probability of dissemination' of an item very often has little to do with whether or not it is 'printed'")

in the sense of that word when it was introduced into the patent statutes in 1836. In any event, interpretation of the words 'printed' and 'publication' to mean 'probability of dissemination' and 'public accessibility' respectively, now seems to render their use in the phrase 'printed publication' somewhat redundant.") *In re Wyer*, 655 F.2d at 226, 210 USPQ at 794.

Thus, one of skill in the art must, after reasonable diligence, be able to access the document. The Parkhill Declaration states in paragraph 4, "The sequence data was publicly available for download via our file transfer protocol (FTP) server." However, an FTP server that is publicly available is of no use unless those in the public actually know that the FTP server exists and what the URL for the FTP server is. Since it is reasonable to assume that the patent attorneys who assisted Dr. Parkhill in the preparation of his Declaration to file in the EPO would have known of this requirement, it is fair to infer that the FTP URL was not advertised to the public. There are any number of reasons that data would be loaded on an FTP server that could be logged onto without a password such as Dr. Parkhill uploading the data to share with collaborators who had individually been emailed the URL.

Furthermore, even if the FTP URL was publicly disclosed, the apparent indexing is not sufficient that one of skill in the art would have been able to find the 1997-12-15-NM.dbs file. As discussed in Section 2128.01(I) of the MPEP:

In In re Hall, general library cataloging and shelving practices showed that a doctoral thesis deposited in university library would have been indexed, cataloged and shelved and thus available to the public before the critical date. Compare *In re Cronyn*, 890 F.2d 1158, 13 USPQ2d 1070 (Fed. Cir. 1989) wherein doctoral theses were shelved and indexed by index cards filed alphabetically by student name and kept in a shoe box in the chemistry library. The index cards only listed the student name and title of the thesis. Two of three judges held that the students' theses were not accessible to the public. The court reasoned that the theses had not been either cataloged or indexed in a meaningful way since thesis could only be found if the researcher's name was known, but the name bears no relationship to the subject of the thesis.

It is by no means clear that one of skill in the art looking for such a file would have been able to navigate the menus of the FTP site to find it under /pub/pathogens/nm/. Furthermore, the

name of the file provides little if any guidance as to its contents. The Parkhill declaration provides no indication as to the state of the FTP site before the priority date of the present application including where the file was located within the directory structure and what other files and directories would have been available. Assuming that logging onto the FTP site begins in the /pub/ directory, there is no indication as to how many directories and files one of skill in the art would have been confronted with upon logging in. Assuming that one of skill in the art chose /pathogen/ from among what is a bewildering array of directories on the site today, again there is no indication as to how many files and directories were in this subdirectory and why one of skill in the art would have chosen /nm/. Further, Dr. Parkhill indicates that the sequence data "was continually updated as new data was generated." Thus, it is unclear how many files would have been in this directory had one visited the site. By way of example, the /old_data/ directory has 1998-01-21-NM.dbs which does not appear to contain Contig 295. The original directories must have included more than just the four files in the /old_data/ directory as Dr. Parkhill indicates that the first shotgun data was released on October 31, 1997, but there is no corresponding 1997-10-31-NM_shotgun.dbs file. Of course, all of this assumes that the file 1997-12-15-NM.dbs was under the directory /pubs/pathogen/nm/. The Parkhill declaration only indicates the files are available over the internet /pubs/pathogen/nm/old_data/. Dr. Parkhill admits that the file was reloaded to where it is now on September 1, 2000 (though the directory /old_data/ bears a time stamp of May 22, 2001), but does not indicate what the directory structure before the priority date of the present application may have been. Absent clear indexing, one of skill in the art even after reasonable diligence would not have been able to find this file given the rather obscure naming.

Examiner has cited no evidence to suggest that the public knew the URL prior to the priority date of the present application, and even if the URL was known, the file was not indexed clearly to allow it to be found after reasonable diligence. Therefore, the file has not been demonstrated to be a "publication" under 35 U.S.C. § 102.

B. The Pending Claims are not Obvious

Assuming that one of skill in the art could find the document, the pending claims would not be obvious nonetheless. The Examiner has asserted as the reason that one of skill in the art would express the polypeptide encoded by the asserted ORF is that, “[o]ne of ordinary skill in the art would have been motivated to produce the instant invention for the expected benefit of producing an antibody to the expressed protein macromolecule in order to study the protein for research purposes since antibodies are made to a protein sometimes without a clear objective for their application as taught by Campbell.” However, section 2107.01(I)(B) of the MPEP states that:

On the other hand, the following are examples of situations that require or constitute carrying out further research to identify or reasonably confirm a “real world” context of use and, therefore, do not define “substantial utilities”:

- (A) Basic research such as studying the properties of the claimed product itself or the mechanisms in which the material is involved;
- (B) A method of treating an unspecified disease or condition;
- (C) A method of assaying for or identifying a material that itself has no specific and/or substantial utility;
- (D) A method of making a material that itself has no specific, substantial, and credible utility; and
- (E) A claim to an intermediate product for use in making a final product that has no specific, substantial and credible utility.

Thus, the Examiner’s asserted reason of expressing the polypeptide to generate antibodies to determine the function is not a real world utility. Without a real world utility, one of skill in the art would not be motivated to actually express the protein. This is clearly discussed in Section 2144 of the MPEP:

If the prior art does not teach any *specific or significant utility* for the disclosed compounds, then the prior art is not sufficient to render structurally similar claims *prima facie* obvious because there is no motivation for one of ordinary skill in the art to make the reference compounds, much less any structurally related compounds. *In re Stremniski*, 444 F.2d 581, 170 USPQ 343 (CCPA 1971).

Thus, *In re Stenniski* addresses the same situation as is presented here. The file 1997-12-15-NM.dbs teaches large fragments of the genome of a *Neisseria meningitidis* serogroup A bacteria. The file 1997-12-15-NM.dbs teaches no utility or even start and stop codons and the only utility suggested by the Examiner is not a real world utility and therefore not a “specific or significant” utility. By contrast, the inventors have annotated the sequence including the start codon, the stop codon and the leader peptide (underlined) as well as identifying a substantial and significant utility as a candidate for inclusion in a vaccine. Thus, 1997-12-15-NM.dbs at best teaches potentially a couple of thousand compounds with no specific or significant utility only one of which is related to the present claims. Just as in *In re Stenniski*, 1997-12-15-NM.dbs cannot render obvious the related polypeptides encoded by ORFs that could be identified therein since the polypeptides similarly lack a “specific or significant” utility.

C. *The Pending Claims are not Obvious Based Upon the Entire Scope of the Art*

As discussed above, the Examiner has asserted as the reason that one of skill in the art would synthesize the asserted ORF is that, “[o]ne of ordinary skill in the art would have been motivated to produce the instant invention for the expected benefit of producing an antibody to the expressed protein macromolecule in order to study the protein for research purposes since antibodies are made to a protein sometimes without a clear objective for their application as taught by Campbell.” However, 1997-12-15-NM.dbs does not disclose even a single open reading frame as there is a complete absence of annotation of any sort. Not a single start or stop codon has been identified. The size of the file is on the order of 2 Megabytes which suggests that the file contains 2 million bases of nucleotide sequence. The sequence data is further broken up into more than three hundred contig blocks. The Examiner in page 2 of the Office Action dated November 11, 2008, recites the factual inquiries under *Graham v. John Deere Co.* the first one of which is: Determine the scope and contents of the prior art. Even limiting oneself to 1997-12-15-NM.dbs, the scope of the art relevant to the motivation cited by the Examiner, i.e., to study an unknown *Neisserial* protein to determine its function, is the entire file and all of the open reading frames that could be identified therein. The Examiner has not indicated why one of skill in the art would be motivated to apply a program that identifies open reading frames to the particular contig identified in the Parkhill declaration as Contig

295 versus any of the over three hundred other contigs in 1997-12-15-NM.dbs. Then after applying the program that identifies open reading frames to select this particular open reading frame over any of the other open reading frames that could be identified in 1997-12-15-NM.dbs. Absent something further, it would not be obvious to select the one particular open reading frame identified by the Examiner out of all possible open reading frames in 1997-12-15-NM.dbs. All of this analysis assumes that one of skill in the art would only have been confronted with one file 1997-12-15-NM.dbs, but as Dr. Parkhill stated, the sequence data was “continually updated as new data was generated.” Thus, there could have been even more sequence data to choose from. Even if the Examiner’s cited motivation of expressing a single polypeptide encoded by an open reading frame to generate antibodies to determine its function were sufficient, one of skill in the art would not have expressed all of the polypeptides encoded by all open reading frames that could be identified in the files available at the Sanger Institute FTP site. As the files lack any guidance that would lead one of skill in the art to the one particular open reading frame. It is only in hindsight based upon the inventors recognition that the claimed polypeptide was a promising candidate for a vaccine, that the Examiner was able to select this open reading frame from all possible that could have been found in 1997-12-15-NM.dbs using a program to identify open reading frames.

Thus, 1997-12-15-NM.dbs does not render the claims obvious as it has not been proven to be a “publication,” and even if it were a “publication,” the lack of a real world utility for either the nucleic acid sequences or the polypeptides encoded by the ORFs that could be identified therein. Thus, applicants respectfully request that the Examiner withdraw the rejection of claims 2, 22-26, and 28.

II. Rejection Under 35 USC 103

Claim 27 is rejected under 35 U.S.C. § 103(a), as allegedly being unpatentable over the disclosure print out of the ‘Contig295’ sequence data from the sequence file 1997-12-15-NM.dbs attached to the Parkhill Declaration in view of the printed output from the NCBI open reading frame finder, Sambrook *et al.*, and Campbell AM.

Applicants respectfully traverse the rejection and its supporting remarks. As discussed above, 1997-12-15-NM.dbs has not been established to be a “publication” under 35 U.S.C. § 102. In addition, the examiner has relied upon the same motivation as for the rejection above in including a pharmaceutically acceptable carrier. As discussed above, since no real world utility is taught in 1997-12-15-NM.dbs for the nucleic acid sequences, it would not be obvious to make polypeptides encoded by ORFs that could be identified therein as the polypeptides would also be lacking in real world utility as the motivation cited by the Examiner is not a real world utility as indicated in the MPEP’s discussion of utility.

Furthermore, pharmaceutically acceptable carriers are those carriers that are safe when used in delivery of drugs and other therapeutics to a human. By contrast, the carriers used in generating antibodies have no such requirement. By way of example, antibodies are typically induced using Freund’s complete adjuvant (FCA) as it is a very potent adjuvant. However, it is also rather toxic and has deleterious effects upon the rabbit or mouse. Thus, FCA is not used in any human vaccine in use today and is an excellent example of a pharmaceutically unacceptable adjuvant used to make antibodies. Thus, since there is no requirement when generating antibodies to a polypeptide in a mouse or rabbit (or other model organism) that the polypeptide be used with pharmaceutically acceptable components such as an adjuvant or carrier, claim 27 is not obvious.

Thus, 1997-12-15-NM.dbs does not render claim 27 obvious as (i) it has not been proven to be a “publication,” (ii) even if it were a “publication,” the lack of a real world utility for either the nucleic acid sequences or the polypeptides encoded by the ORFs that could be found therein with additional work, and (iii) the motivation cited by the Examiner to express a polypeptide to make an antibody does not necessitate use of a pharmaceutically acceptable carrier. Thus, applicants respectfully request that the Examiner withdraw the rejection of claim 27.

CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no. 223002101200. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

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